



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Gaston and Stamler

SERIAL NUMBER : 10/772,374

EXAMINER : Raymond J. Henley, III

FILING DATE : February 6, 2004

ART UNIT : 1614

FOR : THERAPEUTIC USE OF AEROSOLIZED S-NITROSOGLUTATHIONE IN CYSTIC FIBROSIS

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF JONATHAN S. STAMLER UNDER 37 C.F.R. §1.132

I, Jonathan S. Stamler, of 101 Juniper Place, Chapel Hill, North Carolina, 27514, declare and state that:


1. I am a coinventor, together with Benjamin Gaston, in the above-referenced patent application.
2. I received an M.D. from Mount Sinai School of Medicine in New York and then completed my medical residency and fellowship training in both cardiology and pulmonary medicine at Harvard Medical School and the Brigham and Womens Hospital. I hold the position of George Barth Geller Professor for Research in Cardiovascular Diseases, Professor of Medicine and Biochemistry, and an Associate Investigator of the Howard Hughes Medical Institute at the Duke University Medical Center in Durham, North. I have published numerous scientific articles in the field of nitric oxide and nitric oxide donors.
3. I have reviewed the Office Action dated July 13, 2006. I understand that claims 1 and 9 are rejected under 35 U.S.C. §103(a), as being unpatentable over U.S. Patent 6,331,543 to Garvey ('543) in view of U.S. Patent 6,314,956 to Stamler ('956) and further in view of U.S. Patent 5,380,758 to Stamler ('758).

4. I have reviewed the present application in conjunction with the '543, '956, and '758 references.
5. I disagree with the Examiner's assertion that one of ordinary skill in the art would be motivated to combine the '543, '956, and '758 references to reach the present invention and I assert that the cited references do not teach or suggest the unexpected and superior advantages of the claimed administration methods for treating cystic fibrosis.
6. I submit that a skilled artisan would readily recognize a distinction between administration by inhalation and administration to the nasal mucosa and osteomeatal complex. Specifically, the ordinary skilled artisan would recognize that inhalation serves as a route of local administration of a composition or drug to the lungs. The presently claimed invention allows for the systemic delivery of the claimed compositions through absorption by the nasal mucosa and osteomeatal complex which differs from the local administration to the lungs via inhalation taught by the combination of the '543, '956 and '758 patents.
7. I assert that administration to the nasal mucosa and osteomeatal complex provides numerous advantages over other systemic delivery methods, such as parenteral and oral administration, including: non-invasiveness, efficient absorption via highly-vascularized mucosa, rapid onset of action, improved compliance, avoidance of any degradation and/or unwanted metabolism of the drug, which can change the drug's molecular structure and potential for direct delivery to the brain via the tight junctions present in the nasal mucosa and osteomeatal complex.

An advantage of administration of composition or drug to the nasal mucosa and osteomeatal complex is that, typically, a much lower actual dose of the composition or drug can be administered because, compared to oral dosing, the first pass metabolism in the liver and gastrointestinal tract is avoided. Additionally, administration of the claimed compositions to the nasal mucosa and osteomeatal complex in patients suffering from severe cystic fibrosis symptoms; such as, bronchoconstriction, mucus plugging in the lungs or bacterial bronchitis/brochiolitis, will provide rapid relief and

will not be hindered by limitations of local delivery to the lungs via inhalation due to these severe symptoms.

8. I submit that the advantages of the administration route of the instant invention such as the large surface area, porous endothelial membrane, high total blood flow, the avoidance of first-pass metabolism, ready accessibility and rapid systemic absorption following administration of a composition or drug to the nasal mucosa and osteomeatal complex are not suggested by the combination of the '543, '956 and '758 patents.
9. I further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.


Jonathan S. Stamler

Signed this 10/25/06 day of October, 2006

TRA 2213159v.1

Best Available Copy